WHAT IS CLAIMED

1. An isolated bispecific epidermal growth factor receptor (EGFR)/ hepatocyte growth factor receptor (c-Met) antibody, comprising:
   a) a first heavy chain (HC1) comprising a HC1 constant domain 3 (HC1 CH3) and a HC1 variable region 1 (VH1);
   b) a second heavy chain (HC2) comprising a HC2 constant domain 3 (HC2 CH3) and a HC2 variable region 2 (VH2);
   c) a first light chain (LC1) comprising a light chain variable region 1 (VL1); and
   d) a second light chain (LC2) comprising a light chain variable region 2 (VL2), wherein the VH1 and the VL1 pair to form a first antigen-binding site that specifically binds EGFR, the VH2 and the VL2 pair to form a second antigen- binding site that specifically binds c-Met, the HC1 comprises a F405L or a K409R substitution in the HC1 CH3, the HC2 comprises at a F405L or a K409R substitution in the HC2 CH3, the substitution in the HC1 CH3 and the substitution in the HC2 CH3 occurring at different amino acid residue positions, when residue numbering is according to the EU index, and the VH1, the VL1, the VH2 and the VL2 comprise the amino acid sequences of SEQ ID NOs: 189, 190, 193 and 194, respectively.
2. The bispecific antibody of claim 1,

   wherein the antibody inhibits phosphorylation of extracellular signal-related kinases 1 and 2 (ERK1/2) in NCI-H1975 cell line with an IC_{50} value that is at least about 60-fold less when compared to the IC_{50} value of inhibition of phosphorylation of ERK1/2 in NCI-H1975 cell line with a mixture of a control monovalent EGFR antibody comprising a heavy chain 3 (HC3) and a light chain 3 (LC3) and a control monovalent c-Met antibody comprising a heavy chain 4 (HC4) and a light chain 4 (LC4), wherein

   the HC3 and the HC1, the LC3 and the LC1, the HC4 and the HC2, and the LC4 and the LC2 have identical amino acid sequences, respectively, and

   the phosphorylation of ERK1/2 is measured in whole cell lysates by sandwich immunoassay using an anti-phosphoERK1/2 antibody as a capture antibody and an antibody binding to unphosphorylated and phosphorylated ERK1/2 conjugated with an electrochemiluminescent compound as a detection antibody.

3. The bispecific antibody of claims 1 or 2, wherein the antibody inhibits phosphorylation of ERK1/2 with an IC_{50} value of about $2x10^{-9}$ M or less.
4. The bispecific antibody of claim 2 or 3, wherein ERK1 is phosphorylated at residues Thr202 and Tyr204, and ERK2 is phosphorylated at residues Thr185 and Tyr197.
5. The bispecific antibody of any of the claims 1-4,

wherein the antibody inhibits phosphorylation of protein kinase B (AKT) at Ser473 in NCI-H1975 cell line with an IC_{50} value that is at least about 70-fold less when compared to the IC_{50} value of inhibition of phosphorylation of AKT at Ser473 in NCI- H1975 cell line with the mixture of control monovalent EGFR antibody comprising the HC3 and the LC3 and control monovalent c-Met antibody comprising the HC4 and the LC4, wherein

the HC3 and the HC1, the LC3 and the LC1, the HC4 and the HC2, and the LC4 and the LC2 have identical amino acid sequences, respectively, and

phosphorylation of AKT at Ser473 is measured in whole cell lysates by sandwich immunoassay using an antibody binding to unphosphorylated and phosphorylated AKT as a capture antibody and an anti-phospho AKT Ser473 antibody conjugated with an electrochemiluminescent compound as a detection antibody.
6. The bispecific antibody of any of the claims 1-5,

wherein the antibody inhibits phosphorylation of AKT at Thr308 in NCI-H1975 cell line with an IC_{50} value that is at least about 100-fold less when compared to the IC_{50} value of inhibition of phosphorylation of AKT at Thr308 in NCI-H1975 cell line with the mixture of the control monovalent EGFR antibody comprising the HC3 and the LC3 and the control monovalent c-Met antibody comprising the HC4 and the LC4, wherein

the HC3 and the HC1, the LC3 and the LC1, the HC4 and the HC2, and the LC4 and the LC2 have identical amino acid sequences, respectively, and

the phosphorylation of AKT at Thr308 is measured in whole cell lysates by sandwich immunoassay using an antibody binding to unphosphorylated and phosphorylated AKT as a capture antibody and an anti-phospho AKT Thr308 antibody conjugated to an electrochemiluminescent compound as a detection antibody.
7. The bispecific antibody of claim 5 or 6, wherein the antibody inhibits phosphorylation of AKT at Ser473 or at Thr308 with an IC_{50} value of about $1x10^{-9}$ M or less.

8. The bispecific antibody of any of the claims 1-7, wherein the HC1 CH3 comprises the F405L substitution and the HC2 CH3 comprises the K409R substitution.
9. The bispecific antibody of any of the claims 1-8, wherein the HC1 and the HC2 are of IgG1, IgG2, IgG3 or IgG4 isotype.
10. The bispecific antibody of claim 9, wherein the HC1 and the HC2 are of IgG1 isotype.
11. The bispecific antibody of any of the claims 1-10, wherein the HC1, the LC1, the HC2 and the LC2 comprise the amino acid sequences of SEQ ID NOs: 199, 200, 201 and 202, respectively, optionally having a C-terminal lysine removed from the HC1, the HC2, or both the HC1 and the HC2.
12. The bispecific antibody of any of the claims 1-11, wherein the antibody has a biantennary glycan structure with a fucose content of about between 1% to about 15%.
13. The bispecific antibody of claim 1, wherein HC1, LC1, HC2 and LC2 are encoded by synthetic polynucleotides comprising the sequence of SEQ ID NOs: 205, 206, 207 and 208, respectively.
14. An isolated synthetic polynucleotide encoding the HC1, the HC2, the LC1 or the LC2 of claim 1 or 11 or 26.
15. An isolated synthetic polynucleotide comprising the polynucleotide sequence of SEQ ID NOs: 205, 206, 207 or 208.
16. A vector comprising the polynucleotide of claim 14 or 15.
17. An isolated host cell comprising the vector of claim 16.
18. A method of producing the isolated bispecific EGFR/c-Met antibody of claim11, comprising:
    a) combining an isolated monospecific bivalent anti-EGFR antibody comprising two heavy chains of SEQ ID NO: 199 and two light chains of SEQ ID NO: 200 and an isolated monospecific bivalent anti-c-Met antibody comprising two heavy chains of SEQ ID NO: 201 and two light chains of SEQ ID NO: 202 in a mixture of about 1:1 molar ratio;
    b) introducing a reducing agent into the mixture;
    c) incubating the mixture about ninety minutes to about six hours;
    d) removing the reducing agent; and
    e) purifying the bispecific EGFR/c-Met antibody that comprises a first heavy chain of SEQ ID NO: 199 and a second heavy chain of SEQ ID NO: 201, a first light chain of SEQ ID NO: 200 and a second light chain of SEQ ID NO: 202, wherein the first heavy chain of SEQ ID NO: 199 pairs with the first light chain of SEQ ID NO: 200 to form the first binding domain that specifically binds

EGFR, and the second heavy chain of SEQ ID NO: 201 pairs with the second light chain of SEQ ID NO: 202 to form the second binding domain that specifically binds c-Met.

19. The method of claim 18, wherein the reducing agent is 2- mercaptoethanolamine (2-MEA).
20. The method of claim 19, wherein the 2-MEA is present at a concentration of about 25 mM to about 75 mM.
21. The method of claim 20, wherein the incubating step is performed at a temperature of about 25°C to about 37ºC.
22. A pharmaceutical composition comprising the bispecific antibody of any of the claims 1-11 and a pharmaceutically acceptable carrier.
23. A bispecific antibody of any of the claims 1-11 for therapy.

WHAT IS CLAIMED

1. An isolated bispecific epidermal growth factor receptor (EGFR)/ hepatocyte growth factor receptor (c-Met) antibody, comprising:
   a) a first heavy chain (HC1);
   b) a first light chain (LC1);
   c) a second heavy chain (HC2); and
   d) a second light chain (LC2); wherein the HC1, the LC1, the HC2 and the LC2 comprise amino acid sequences of SEQ ID NOs: 199, 200, 201 and 202, respectively.

2. A pharmaceutical composition comprising the bispecific antibody of claim 1 and a pharmaceutically acceptable carrier.

3. The bispecific antibody of claim 1 for use in therapy.